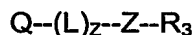


## CLAIMS

What is claimed is:

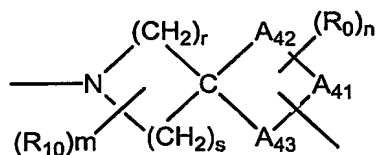
1. A method for treating, preventing or inhibiting tumor cell metastasis in a subject comprising administering to the subject in need of such therapy a therapeutically effective amount of an activated  $\alpha_{IIb}\beta_3$  receptor antagonist.
2. The method of claim 1, wherein the tumor cell metastasis targets an organ system of the subject.
3. The method of claim 2, wherein the tumor cell metastasis targets a skeletal system of the subject.
4. The method of claim 3, wherein the tumor cell metastasis targets a bone of the subject skeletal system.
5. The method of claim 3, wherein the tumor cell metastasis targets a bone cell of the subject skeletal system.
6. The method of claim 1, wherein the antagonist is a platelet-specific activated  $\alpha_{IIb}\beta_3$  receptor antagonist.
7. The method of claim 1, wherein the platelet-specific activated  $\alpha_{IIb}\beta_3$  receptor antagonist is a spiro compound.
8. The method of claim 7, wherein the spiro compound is represented by the formula:



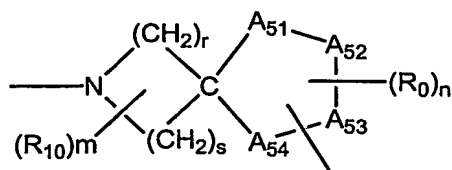
wherein

Z is a spirocyclic nucleus selected from the group consisting of Nucleus (A), (B), (C), or (D) represented by the formulas:

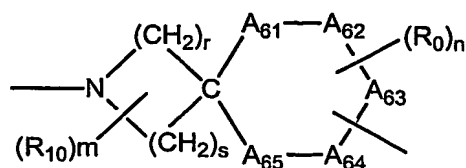
Nucleus (A)



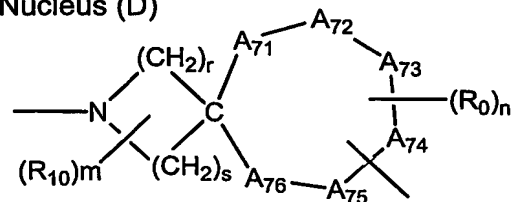
Nucleus (B)



Nucleus (C)



Nucleus (D)



wherein

the group  $Q-(L)_z$  -- is bound to the nitrogen containing ring of nuclei (A), (B), (C), or (D) and the group  $R_3$  is bound to the ring formed by the groups  $A_{41}$ ,  $A_{42}$ ,  $A_{43}$ ,  $A_{51}$ ,  $A_{52}$ ,  $A_{53}$ ,  $A_{54}$ ,  $A_{61}$ ,  $A_{62}$ ,  $A_{63}$ ,  $A_{64}$ ,  $A_{65}$ ,  $A_{71}$ ,  $A_{72}$ ,  $A_{73}$ ,  $A_{74}$ ,  $A_{75}$ , or  $A_{76}$ ; or

the group  $R_3$  is bound to the nitrogen containing ring and the group  $Q-(L)_z$  -- is bound to the ring formed by the groups  $A_{41}$ ,  $A_{42}$ ,  $A_{43}$ ,  $A_{51}$ ,  $A_{52}$ ,  $A_{53}$ ,  $A_{54}$ ,  $A_{61}$ ,  $A_{62}$ ,  $A_{63}$ ,  $A_{64}$ ,  $A_{65}$ ,  $A_{71}$ ,  $A_{72}$ ,  $A_{73}$ ,  $A_{74}$ ,  $A_{75}$ , or  $A_{76}$ ;

$r$  and  $s$  are independently a number from zero to 5 with the proviso that not both  $r$  or  $s$  are 0 and  $(r+s)$  is not more than 6, and  $z$  is zero or one;

atoms  $A_{41}$ ,  $A_{42}$ ,  $A_{43}$ ,  $A_{51}$ ,  $A_{52}$ ,  $A_{53}$ ,  $A_{54}$ ,  $A_{61}$ ,  $A_{62}$ ,  $A_{63}$ ,  $A_{64}$ ,  $A_{65}$ ,  $A_{71}$ ,  $A_{72}$ ,  $A_{73}$ ,  $A_{74}$ ,  $A_{75}$ , or  $A_{76}$  are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one of said atoms is carbon;

provided that the hydrogens of the nitrogen containing part of the spirocycle Z may be substituted by a number of  $m$  substituents  $R_{10}$ , wherein;

$m$  is a number from zero to  $(r+s)$ ; and

$R_{10}$  is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo,  $==O$ , or  $==S$ , with the proviso that only one or two  $R_{10}$  may be  $==O$  or  $==S$ ;

$n$  is a number from zero to 3 in Z of having nuclei (A), or a number from zero to 4 in Z having nuclei (B), a number from zero to 5 in Z having nuclei (C), or a number from zero to 6 in Z having nuclei (D);

$R_0$  is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo,  $==O$ , or  $==S$ , with the proviso that only one or two  $R_0$  may be  $==O$  or  $==S$ ; and

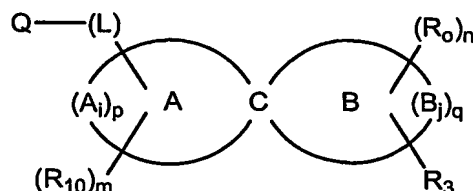
--(L)-- is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

$Q$  is a basic group containing one or more basic radicals; and

$R_3$  is an acidic group containing one or more acid radicals;

or a pharmaceutically acceptable salt, solvate or pro-drug thereof.

9. The method of claim 7, wherein the spiro compound is represented by the formula:



wherein

atoms  $A_i$  and  $B_j$  are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one atom of  $A_i$  is carbon, and at least one atom  $B_j$  is carbon;

optionally, the rings of the spirobicycle formed by  $A_i$  and  $B_j$ , respectively, are partly unsaturated;

$p$  and  $q$  are independently numbers from 2 to 6;

$m$  is a number from zero to  $p$ ;

$R_{10}$  is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo,  $\text{===O}$ , or  $\text{===S}$ , with the proviso that only one  $R_{10}$  may be  $\text{===O}$  or  $\text{===S}$ , if  $p$  is 2 or one or two  $R_{10}$  may be  $\text{===O}$  or  $\text{===S}$ , if  $p$  is a number from 3 to 6;

$n$  is the number from zero to  $q$ ;

$R_o$  is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo,  $\text{===O}$ , or  $\text{===S}$ , with the proviso that only one  $R_o$  may be  $\text{===O}$  or  $\text{===S}$ , if  $q$  is 2 or one or two  $R_o$  may be  $\text{===O}$  or  $\text{===S}$ , if  $q$  is a number from 3 to 6;

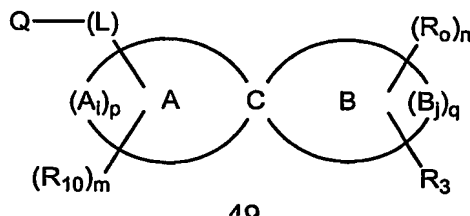
$\text{--(L)--}$  is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

$Q$  is a basic group containing one or more basic radicals; and

$R_3$  is an acidic group containing one or more acid radicals;

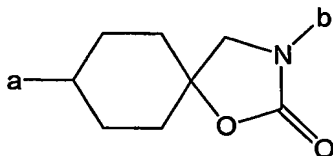
or a pharmaceutically-acceptable salt, solvate or pro-drug thereof..

10. The method of claim 7, wherein the spiro compound is represented by the formula:



wherein

the spirocycle having (A)<sub>p</sub>, C, and (B)<sub>q</sub> is



m is a number from zero to 9;

R<sub>10</sub> is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, or sulfo;

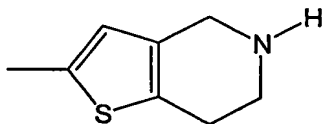
n is a number from zero to 2;

R<sub>0</sub> is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, or sulfo;

wherein Q--(L) is attached at a, and R<sub>3</sub> is attached at b;

--(L)-- is a bond or a substituted or unsubstituted chain selected from the group consisting of CO, CO(C<sub>1</sub>-C<sub>6</sub> alkyl), O(C<sub>1</sub>-C<sub>6</sub> alkyl), NHCO, and C<sub>1</sub>-C<sub>6</sub> alkyl;

Q is a basic group selected from the group consisting of amino, imino, amidino, hydroxyamidino, N-alkylamidine, N,N'-dialkylamidine, N-arylamidine, aminomethyleneamino, aminomethylamino, guanidino, aminoguanidino, alkylamino, dialkylamino, trialkylamino, alkylideneamino, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, indoliziny, isoindolyl, 3H-indolyl, indolyl, 1H-indazolyl, purinyl, 4H-quinoliziny, isoquinolyl, quinolyl, phthalazinyl, naphthyridinyl, quinoxaliny, quinazolinyl, cinnolinyl, amide, thioamide, benzamidino, pteridinyl, 4aH-carbozoly, carbozoly, beta-carbolinyl, phenanthridinyl, acridinyl, phenanthrolinyl, phenazinyl, phenarsazinyl, phenothiazinyl, pyrrolinyl, imidazolidinyl, imidazoliny, pyrazolidinyl, pyrazolinyl, piperidyl, piperazinyl, indoliny, isoindoliny, quinuclidinyl, morpholinyl, any of the foregoing radicals substituted on a benzene ring, optionally substituted with R<sub>2c</sub>, wherein R<sub>2c</sub> is hydrogen or halogen and any of the foregoing radicals substituted by amino, imino, amidino, hydroxyamidino, aminomethyleneamino, iminomethylamino, guanidino, alkylamino, dialkylamino, trialkylamino, tetrahydroisoquinoline, dihydroisoindole, alkylideneamino or



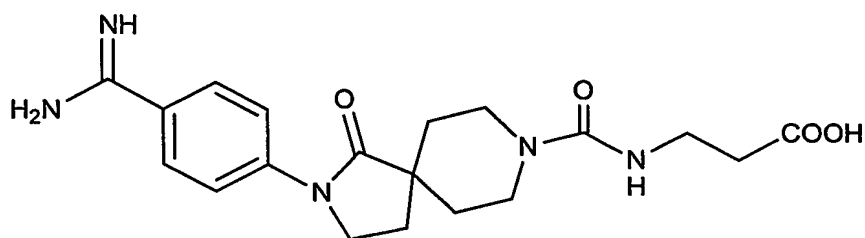
; and

$R_3$  is an acidic group selected from the group consisting of  $\text{CO}_2 R_5$ ,  $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CO}_2 R_5$ ,  $\text{CO}(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CO}_2 R_5$ ,  $\text{CONH}(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CO}_2 R_5$ ,  $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CH}(\text{NHR}_4)\text{CO}_2 R_5$ ,  $\text{CO}(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CH}(\text{NHR}_4)\text{CO}_2 R_5$ , or  $\text{CONH}(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CH}(\text{NHR}_4)\text{CO}_2 R_5$ , wherein  $R_4$  is  $\text{SO}_2 (\text{C}_1\text{-C}_6 \text{ alkyl})$ ,  $\text{SO}_2 \text{ aryl}$ , or  $\text{SO}_2 (\text{substituted aryl})$ ; and

$R_5$  is hydrogen,  $\text{C}_1\text{-C}_6 \text{ alkyl}$ , aryl, or substituted aryl;

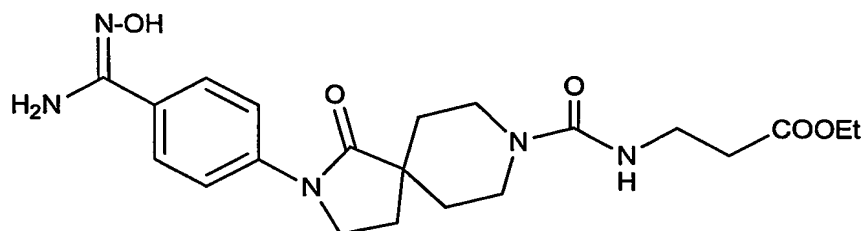
or a pharmaceutically acceptable salt, solvate or pro-drug thereof.

11. The method of claim 7, wherein the spiro compound is represented by the formula:



or a pro-drug thereof.

12. The method of claim 11, wherein the pro-drug is represented by the formula:



13. A method for preventing or inhibiting tumor cell formation in a subject comprising administering to the subject in need of such therapy a therapeutically effective amount of an activated  $\alpha_{1\text{Ib}}\beta_3$  receptor antagonist.

14. The method of claim 13, wherein the tumor cell the tumor cell is formed in an organ system of the subject.

15. The method of claim 14, wherein the tumor cell the tumor cell is formed in a skeletal system of the subject.

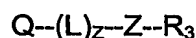
16. The method of claim 15, wherein the tumor cell the tumor cell is formed in a bone of the subject skeletal system.

17. The method of claim 15, wherein the tumor cell the tumor cell is formed in a bone cell of the subject skeletal system.

18. The method of claim 13, wherein the antagonist is a platelet-specific activated  $\alpha_{IIb}\beta_3$  receptor antagonist.

19. The method of claim 18, wherein the platelet-specific activated  $\alpha_{IIb}\beta_3$  receptor antagonist is a spiro compound.

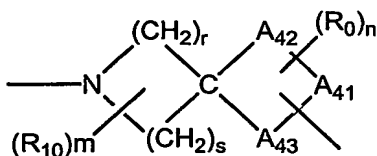
20. The method of claim 19, wherein the spiro compound is represented by the formula:



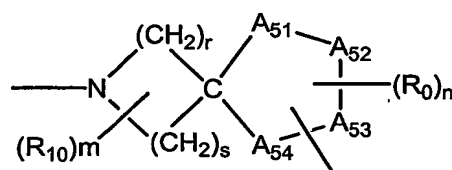
wherein

Z is a spirocyclic nucleus selected from the group consisting of Nucleus (A), (B), (C), or (D) represented by the formulas:

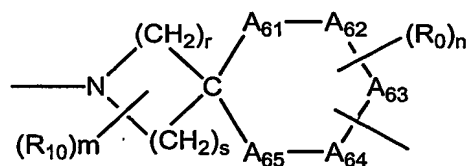
Nucleus (A)



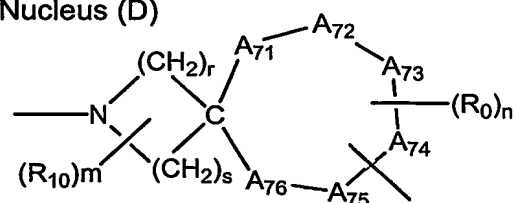
Nucleus (B)



Nucleus (C)



Nucleus (D)



wherein

the group Q--(L)<sub>Z</sub> -- is bound to the nitrogen containing ring of nuclei (A), (B), (C), or (D) and the group R<sub>3</sub> is bound to the ring formed by the groups A<sub>41</sub>, A<sub>42</sub>, A<sub>43</sub>, A<sub>51</sub>, A<sub>52</sub>, A<sub>53</sub>, A<sub>54</sub>, A<sub>61</sub>, A<sub>62</sub>, A<sub>63</sub>, A<sub>64</sub>, A<sub>65</sub>, A<sub>71</sub>, A<sub>72</sub>, A<sub>73</sub>, A<sub>74</sub>, A<sub>75</sub>, or A<sub>76</sub>; or

the group R<sub>3</sub> is bound to the nitrogen containing ring and the group Q--(L)<sub>Z</sub> -- is bound to the ring formed by the groups A<sub>41</sub>, A<sub>42</sub>, A<sub>43</sub>, A<sub>51</sub>, A<sub>52</sub>, A<sub>53</sub>, A<sub>54</sub>, A<sub>61</sub>, A<sub>62</sub>, A<sub>63</sub>, A<sub>64</sub>, A<sub>65</sub>, A<sub>71</sub>, A<sub>72</sub>, A<sub>73</sub>, A<sub>74</sub>, A<sub>75</sub>, or A<sub>76</sub>;

r and s are independently a number from zero to 5 with the proviso that not both r or s are 0 and (r+s) is not more than 6, and z is zero or one;

atoms  $A_{41}$ ,  $A_{42}$ ,  $A_{43}$ ,  $A_{51}$ ,  $A_{52}$ ,  $A_{53}$ ,  $A_{54}$ ,  $A_{61}$ ,  $A_{62}$ ,  $A_{63}$ ,  $A_{64}$ ,  $A_{65}$ ,  $A_{71}$ ,  $A_{72}$ ,  $A_{73}$ ,  $A_{74}$ ,  $A_{75}$ , or  $A_{76}$  are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one of said atoms is carbon;

the hydrogens of the nitrogen containing part of the spirocycle Z may be substituted by a number of m substituents  $R_{10}$ , wherein;

m is a number from zero to (r+s); and

$R_{10}$  is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo,  $\text{===O}$ , or  $\text{===S}$ , with the proviso that only one or two  $R_{10}$  may be  $\text{===O}$  or  $\text{===S}$ ;

n is a number from zero to 3 in Z of having nuclei (A), or a number from zero to 4 in Z having nuclei (B), a number from zero to 5 in Z having nuclei (C), or a number from zero to 6 in Z having nuclei (D);

$R_0$  is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo,  $\text{===O}$ , or  $\text{===S}$ , with the proviso that only one or two  $R_0$  may be  $\text{===O}$  or  $\text{===S}$ ; and

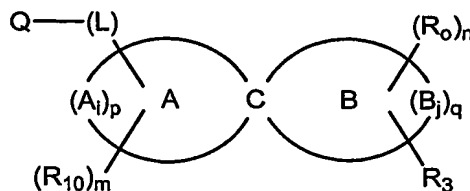
--(L)-- is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

Q is a basic group containing one or more basic radicals; and

$R_3$  is an acidic group containing one or more acid radicals;

or a pharmaceutically-acceptable salt, solvate or pro-drug thereof.

21. The method of claim 19, wherein the spiro compound is represented by the formula:



wherein

atoms  $A_i$  and  $B_j$  are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one atom of  $A_i$  is carbon, and at least one atom of  $B_j$  is carbon;

optionally, the rings of the spirobicycle formed by  $A_i$  and  $B_j$ , respectively, are partly unsaturated;

p and q are independently numbers from 2 to 6;

m is a number from zero to p;

$R_{10}$  is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo,  $\text{===O}$ , or  $\text{===S}$ , with the proviso that only one  $R_{10}$  may be  $\text{===O}$  or  $\text{===S}$ , if p is 2 or one or two  $R_{10}$  may be  $\text{===O}$  or  $\text{===S}$ , if p is a number from 3 to 6;

n is the number from zero to q;

$R_0$  is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo,  $\text{===O}$ , or  $\text{===S}$ , with the proviso that only one  $R_0$  may be  $\text{===O}$  or  $\text{===S}$ , if q is 2 or one or two  $R_0$  may be  $\text{===O}$  or  $\text{===S}$ , if q is a number from 3 to 6;

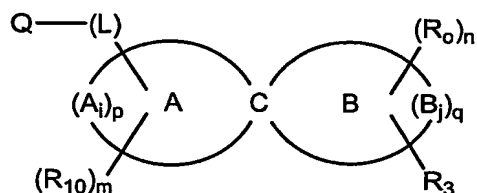
--(L)-- is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

Q is a basic group containing one or more basic radicals; and

$R_3$  is an acidic group containing one or more acid radicals;

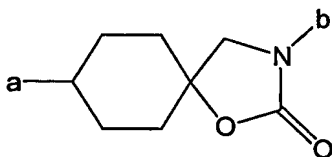
or a pharmaceutically-acceptable salt, solvate or pro-drug thereof..

22. The method of claim 19, wherein the spiro compound is represented by the formula:



wherein

the spirocycle having  $(A_i)_p$ , C, and  $(B_j)_q$  is



m is a number from zero to 9;

$R_{10}$  is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, or sulfo;

n is a number from zero to 2;

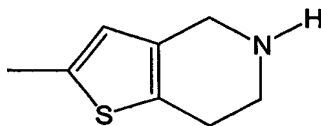


$R_0$  is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, or sulfo;

wherein Q--(L) is attached at a, and  $R_3$  is attached at b;

--(L)-- is a bond or a substituted or unsubstituted chain selected from the group consisting of CO, CO(C<sub>1</sub>-C<sub>6</sub> alkyl), O(C<sub>1</sub>-C<sub>6</sub> alkyl), NHCO, and C<sub>1</sub>-C<sub>6</sub> alkyl;

Q is a basic group selected from the group consisting of amino, imino, amidino, hydroxyamidino, N-alkylamidino, N,N'-dialkylamidino, N-arylamidino, aminomethyleneamino, aminomethylamino, guanidino, aminoguanidino, alkylamino, dialkylamino, trialkylamino, alkylideneamino, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, indoliziny, isoindolyl, 3H-indolyl, indolyl, 1H-indazolyl, purinyl, 4H-quinoliziny, isoquinolyl, quinolyl, phthalazinyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, amide, thioamide, benzamidino, pteridinyl, 4aH-carbozoyl, carbozoyl, beta-carbolinyl, phenanthridinyl, acridinyl, phenanthrolinyl, phenazinyl, phenarsazinyl, phenothiazinyl, pyrrolinyl, imidazolidinyl, imidazoliny, pyrazolidinyl, pyrazolinyl, piperidyl, piperazinyl, indolinyl, isoindolinyl, quinuclidinyl, morpholinyl, any of the foregoing radicals substituted on a benzene ring, optionally substituted with  $R_{2c}$ , wherein  $R_{2c}$  is hydrogen or halogen and any of the foregoing radicals substituted by amino, imino, amidino, hydroxyamidino, aminomethyleneamino, iminomethylamino, guanidino, alkylamino, dialkylamino, trialkylamino, tetrahydroisoquinoline, dihydroisoindole, alkylideneamino or



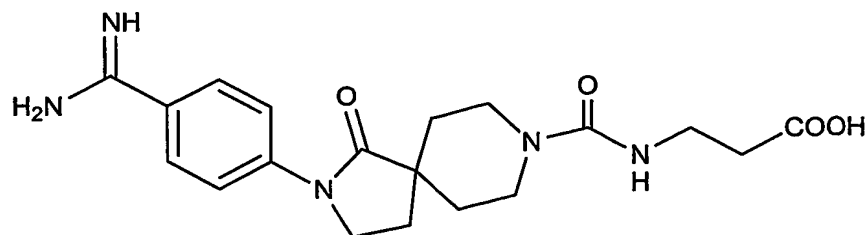
; and

$R_3$  is an acidic group selected from the group consisting of CO<sub>2</sub>  $R_5$ , (C<sub>1</sub>-C<sub>6</sub> alkyl)CO<sub>2</sub>  $R_5$ , CO(C<sub>1</sub>-C<sub>6</sub> alkyl)CO<sub>2</sub>  $R_5$ , CONH(C<sub>1</sub>-C<sub>6</sub> alkyl)CO<sub>2</sub>  $R_5$ , (C<sub>1</sub>-C<sub>6</sub> alkyl)CH(NHR<sub>4</sub>)CO<sub>2</sub>  $R_5$ , CO(C<sub>1</sub>-C<sub>6</sub> alkyl)CH(NHR<sub>4</sub>)CO<sub>2</sub>  $R_5$ , or CONH(C<sub>1</sub>-C<sub>6</sub> alkyl)CH(NHR<sub>4</sub>)CO<sub>2</sub>  $R_5$ , wherein  $R_4$  is SO<sub>2</sub> (C<sub>1</sub>-C<sub>6</sub> alkyl), SO<sub>2</sub> aryl, or SO<sub>2</sub> (substituted aryl); and

$R_5$  is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, or substituted aryl;

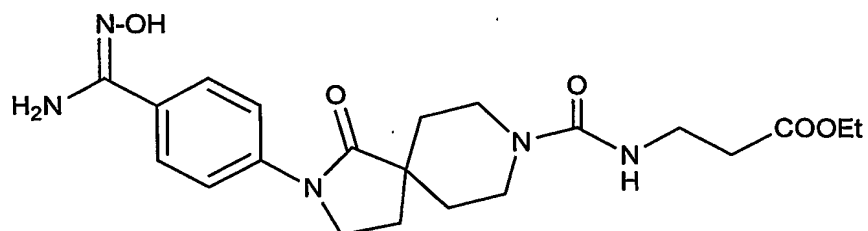
or a pharmaceutically-acceptable salt, solvate or pro-drug thereof.

23. The method of claim 19, wherein the spiro compound is represented by the formula:



or a pro-drug thereof.

24. The method of claim 23, wherein the pro-drug is represented by the formula:



25. A method for destroying a tumor in a subject comprising administering to the subject in need of such therapy a therapeutically effective amount of an activated  $\alpha_{IIb}\beta_3$  receptor antagonist.

26. The method of claim 25, wherein the tumor cell resides in an organ system of the subject.

27. The method of claim 26, wherein the tumor cell resides in a skeletal system of the subject.

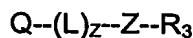
28. The method of claim 27, wherein the tumor cell resides in a bone of the subject skeletal system.

29. The method of claim 27, wherein the tumor cell resides in a bone cell of the subject skeletal system.

30. The method of claim 25, wherein the antagonist is a platelet-specific activated  $\alpha_{IIb}\beta_3$  receptor antagonist.

31. The method of claim 30, wherein the platelet-specific activated  $\alpha_{IIb}\beta_3$  receptor antagonist is a spiro compound.

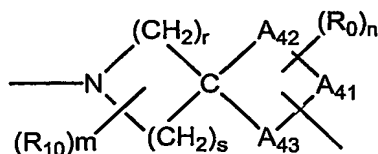
32. The method of claim 31, wherein the spiro compound is represented by the formula:



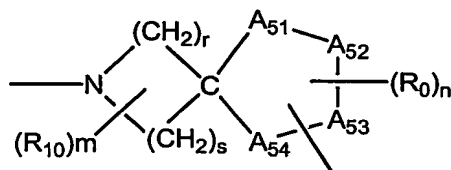
wherein

Z is a spirocyclic nucleus selected from the group consisting of Nucleus (A), (B), (C), or (D) represented by the formulas:

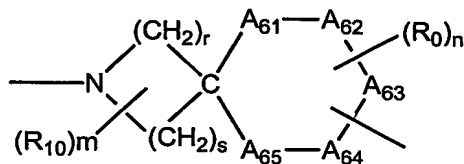
Nucleus (A)



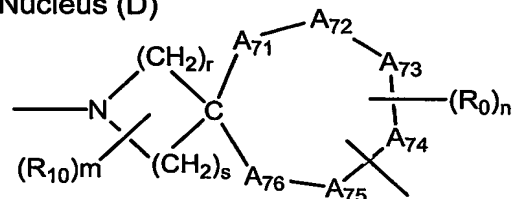
Nucleus (B)



Nucleus (C)



Nucleus (D)



wherein

the group Q--(L)<sub>z</sub> -- is bound to the nitrogen containing ring of nuclei (A), (B), (C), or (D) and the group R<sub>3</sub> is bound to the ring formed by the groups A<sub>41</sub>, A<sub>42</sub>, A<sub>43</sub>, A<sub>51</sub>, A<sub>52</sub>, A<sub>53</sub>, A<sub>54</sub>, A<sub>61</sub>, A<sub>62</sub>, A<sub>63</sub>, A<sub>64</sub>, A<sub>65</sub>, A<sub>71</sub>, A<sub>72</sub>, A<sub>73</sub>, A<sub>74</sub>, A<sub>75</sub>, or A<sub>76</sub>; or

the group R<sub>3</sub> is bound to the nitrogen containing ring and the group Q--(L)<sub>z</sub> -- is bound to the ring formed by the groups A<sub>41</sub>, A<sub>42</sub>, A<sub>43</sub>, A<sub>51</sub>, A<sub>52</sub>, A<sub>53</sub>, A<sub>54</sub>, A<sub>61</sub>, A<sub>62</sub>, A<sub>63</sub>, A<sub>64</sub>, A<sub>65</sub>, A<sub>71</sub>, A<sub>72</sub>, A<sub>73</sub>, A<sub>74</sub>, A<sub>75</sub>, or A<sub>76</sub>;

r and s are independently a number from zero to 5 with the proviso that not both r or s are 0 and (r+s) is not more than 6, and z is zero or one;

atoms A<sub>41</sub>, A<sub>42</sub>, A<sub>43</sub>, A<sub>51</sub>, A<sub>52</sub>, A<sub>53</sub>, A<sub>54</sub>, A<sub>61</sub>, A<sub>62</sub>, A<sub>63</sub>, A<sub>64</sub>, A<sub>65</sub>, A<sub>71</sub>, A<sub>72</sub>, A<sub>73</sub>, A<sub>74</sub>, A<sub>75</sub>, or A<sub>76</sub> are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one of said atoms is carbon;

the hydrogens of the nitrogen containing part of the spirocycle Z may be substituted by a number of m substituents R<sub>10</sub>, wherein;

m is a number from zero to (r+s); and

R<sub>10</sub> is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo, ==O, or ==S, with the proviso that only one or two R<sub>10</sub> may be ==O or ==S;

n is a number from zero to 3 in Z of having nuclei (A), or a number from zero to 4 in Z having nuclei (B), a number from zero to 5 in Z having nuclei (C), or a number from zero to 6 in Z having nuclei (D);

$R_0$  is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo,  $\text{===O}$ , or  $\text{===S}$ , with the proviso that only one or two  $R_0$  may be  $\text{===O}$  or  $\text{===S}$ ; and

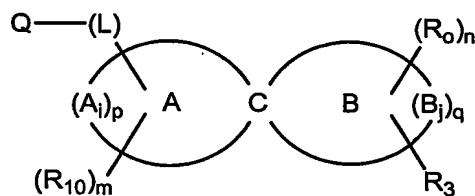
--(L)-- is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

Q is a basic group containing one or more basic radicals; and

$R_3$  is an acidic group containing one or more acid radicals;

or a pharmaceutically-acceptable salt, solvate or pro-drug thereof.

33. The method of claim 31, wherein the spiro compound is represented by the formula:



wherein

atoms  $A_i$  and  $B_j$  are independently selected from carbon, nitrogen, oxygen or sulfur, provided that at least one atom of  $A_i$  is carbon, and at least one atom  $B_j$  is carbon;

optionally, the rings of the spirobicycle formed by  $A_i$  and  $B_j$ , respectively, are partly unsaturated;

p and q are independently numbers from 2 to 6;

m is a number from zero to p;

$R_{10}$  is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, sulfo,  $\text{===O}$ , or  $\text{===S}$ , with the proviso that only one  $R_{10}$  may be  $\text{===O}$  or  $\text{===S}$ , if p is 2 or one or two  $R_{10}$  may be  $\text{===O}$  or  $\text{===S}$ , if p is a number from 3 to 6;

n is the number from zero to q;

$R_0$  is the same or different and is a non-interfering substituent independently selected from hydrogen, alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano,

halo, nitro, sulfo,  $\text{===O}$ , or  $\text{===S}$ , with the proviso that only one  $R_0$  may be  $\text{===O}$  or  $\text{===S}$ , if  $q$  is 2 or one or two  $R_0$  may be  $\text{===O}$  or  $\text{===S}$ , if  $q$  is a number from 3 to 6;

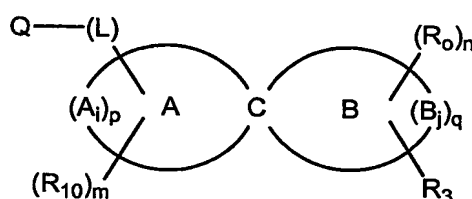
--(L)-- is a bond or a divalent substituted or unsubstituted chain of from 1 to 10 atoms selected from the group consisting of carbon, nitrogen, sulfur, and oxygen;

$Q$  is a basic group containing one or more basic radicals; and

$R_3$  is an acidic group containing one or more acid radicals;

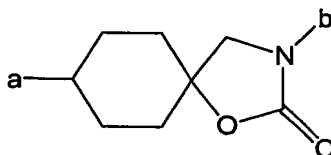
or a pharmaceutically-acceptable salt, solvate or pro-drug thereof..

34. The method of claim 31, wherein the spiro compound is represented by the formula:



wherein

the spirocycle having  $(A)_p$ , C, and  $(B)_q$  is



$m$  is a number from zero to 9;

$R_{10}$  is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, or sulfo;

$n$  is a number from zero to 2;

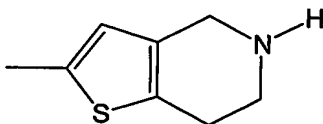
$R_0$  is the same or different and is a non-interfering substituent independently selected from alkyl, halosubstituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, hydroxy, alkoxy, arylalkoxy, amino, substituted amino, carbamoyl, carboxy, acyl, cyano, halo, nitro, or sulfo;

wherein  $Q$ --(L) is attached at  $a$ , and  $R_3$  is attached at  $b$ ;

--(L)-- is a bond or a substituted or unsubstituted chain selected from the group consisting of CO, CO( $C_1$ - $C_6$  alkyl), O( $C_1$ - $C_6$  alkyl), NHCO, and  $C_1$ - $C_6$  alkyl;

$Q$  is a basic group selected from the group consisting of amino, imino, amidino, hydroxyamidino, N-alkylamidino, N,N'-dialkylamidino, N-arylamidino, aminomethyleneamino, aminomethylamino, guanidino, aminoguanidino, alkylamino, dialkylamino, trialkylamino, alkylideneamino, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, indoliziny, isoindolyl, 3H-indolyl, indolyl, 1H-indazolyl, purinyl, 4H-quinoliziny, isoquinolyl, quinolyl,

phthalazinyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, amide, thioamide, benzamidino, pteridinyl, 4aH-carbozoyl, carbozoyl, beta-carbolinyl, phenanthridinyl, acridinyl, phenanthrolinyl, phenazinyl, phenarsazinyl, phenothiazinyl, pyrrolinyl, imidazolidinyl, imidazolyl, pyrazolidinyl, pyrazolyl, piperidyl, piperazinyl, indolyl, isoindolyl, quinuclidinyl, morpholinyl, any of the foregoing radicals substituted on a benzene ring, optionally substituted with  $R_{2c}$ , wherein  $R_{2c}$  is hydrogen or halogen and any of the foregoing radicals substituted by amino, imino, amidino, hydroxyamidino, aminomethyleneamino, iminomethylamino, guanidino, alkylamino, dialkylamino, trialkylamino, tetrahydroisoquinoline, dihydroisoindole, alkylideneamino or



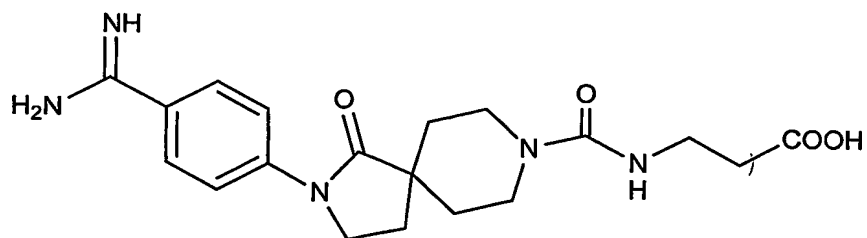
; and

$R_3$  is an acidic group selected from the group consisting of  $\text{CO}_2 R_5$ ,  $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CO}_2 R_5$ ,  $\text{CO}(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CO}_2 R_5$ ,  $\text{CONH}(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CO}_2 R_5$ ,  $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CH}(\text{NHR}_4)\text{CO}_2 R_5$ ,  $\text{CO}(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CH}(\text{NHR}_4)\text{CO}_2 R_5$ , or  $\text{CONH}(\text{C}_1\text{-C}_6 \text{ alkyl})\text{CH}(\text{NHR}_4)\text{CO}_2 R_5$ , wherein  $R_4$  is  $\text{SO}_2 (\text{C}_1\text{-C}_6 \text{ alkyl})$ ,  $\text{SO}_2 \text{ aryl}$ , or  $\text{SO}_2 (\text{substituted aryl})$ ; and

$R_5$  is hydrogen,  $\text{C}_1\text{-C}_6 \text{ alkyl}$ , aryl, or substituted aryl;

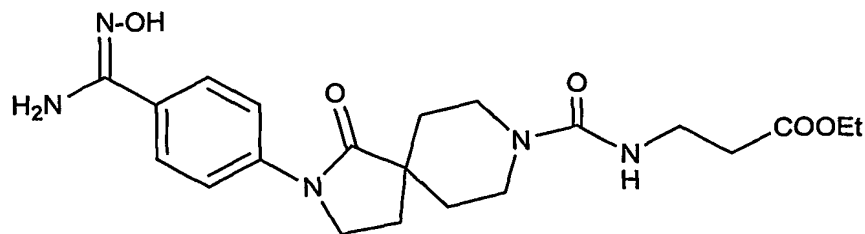
or a pharmaceutically-acceptable salt, solvate or pro-drug thereof.

35. The method of claim 31, wherein the spiro compound is represented by the formula:



or a pro-drug thereof.

36. The method of claim 35, wherein the pro-drug is represented by the formula:



37. A method for treating, preventing or inhibiting tumor cell metastasis to bone in a subject comprising replacing substantially all bone marrow affected by tumor cell metastasis transplant in the subject, wherein said bone marrow is replaced with  $\beta_3^{-/-}$  bone marrow.

38. A method for treating, preventing or reversing tumor metastasis or formation comprising modulating  $\beta_3$  integrin expression.

39. The method of claim 38, wherein the modulating  $\beta_3$  integrin expression  
5 comprises decreasing the  $\beta_3$  integrin expression in a mammalian cell.

40. The method of claim 39, wherein decreasing the expression comprises transforming the cell to express a polynucleotide anti-sense to at least a portion of an endogenous polynucleotide encoding  $\beta_3$  integrin.

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41. The method of claim 39, wherein decreasing the expression comprises transfecting the cell with a polynucleotide anti-sense to at least a portion of an endogenous polynucleotide encoding  $\beta_3$  integrin.

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42. The method of claim 39, wherein decreasing the expression comprises transfecting a cell with a siRNA targeting at least a portion of an endogenous polynucleotide encoding  $\beta_3$  integrin.